PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 10 July 2001 (10.07.01)	
International application No. PCT/EP00/10084	**Applicant's or agent's file reference** A000005-PCT2
International filing date (day/month/year) 09 October 2000 (09.10.00)	**Priority date** (day/month/year) 07 October 1999 (07.10.99)
Applicant HUGHES, John et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

27 April 2001 (27.04.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Pascal Piriou

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
A000005-PCT2		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/10084	09/10/2000	07/10/1999
International Patent Classification (IPC) or national classification and IPC		
A61K31/195		
Applicant		
WARNER-LAMBERT COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27/04/2001	23.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pilling, S Telephone No. +49 89 2399 8461

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/10084

I. Basis f the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-12 as originally filed

Claims, No.:

1-11 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 1-9.

because:

   ☒ the said international application, or the said claims Nos. 1-9 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reason d statement under Articl 35(2) with r gard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-11

	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	10,11 (for Claims 1-9 see the comments under Item V)
	No:	Claims	

2. Citations and explanations
see separate sheet

Re It m III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1 to 9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2. The present application relates to the treatment of psychiatric disorders using a synergistic combination of an NK_1 receptor antagonist and a GABA analogue.

3. Claims 1 to 9 relate to methods of treatment of the human or animal body by therapy. In this regard, for the assessment of these claims with respect to industrial applicability, no unified criteria exist in the PCT. Furthermore, patentability can be dependent on the formulation of the claims. The EPO, for example does not recognize as industrially applicable, the subject matter of claims directed to a method of treatment of the human or animal body or to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D5 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

5. None of the documents cited in the ISR discloses treatment of psychiatric disorders using a combination of an NK_1 receptor antagonist and a GABA analogue. Thus, the subject matter of the present claims is new (Article 33(2) PCT).

6. The closest prior art in respect of the present claims appears to be any of documents D1 to D5. These documents show that the separate use of either (i) NK_1 receptor analogues (see documents D1 to D2) or (ii) GABA analogues such as gabapentin or pregabalin (see documents D3 to D5) for the treatment of psychiatric disorders such as anxiety, depression and panic is known. Despite numerous references in the present description to a synergistic effect associated with the combined use of these active agents in treating psychiatric disorders, there seems to be no clear evidence therein to support the existence of any such synergistic effect. In particular, the method of present Example 1 only appears to have been carried out using the Applicant's preferred NK_1 receptor antagonist, *i.e.* CI-1021. There seem to be no experimental results relating to the combined use of the latter compound with GABA analogues. Hence, it is considered that the alleged synergistic effect has not yet been made credible and cannot presently be used to support inventive step of the present claims.

7. Hence, the objective technical problem to be solved by the subject matter of the present application appears to be "*how to provide alternative compositions for the treatment of psychiatric disorders*". The Applicant is advised that in general it is not considered inventive to combine active agents for the treatment of a particular disease wherein (i) said active agents were individually known for the treatment of said disease and (ii) wherein the combination thereof has no surprising technical effects, *e.g.* synergistic effect(s). In this regard, it is common general knowledge in the medical art that treatments may be combined and it would be expected that (at least additive) therapeutic benefits would be associated with the use of such combined treatment. Hence, in the absence of any proven surprising technical effect(s) associated with the use of the NK_1 receptor antagonists in combination with the GABA analogues to treat psychiatric disorders, it is considered that the present claims merely define obvious combined treatments. Thus, the subject matter of Claims 1 to 11 is not inventive (Article 33(3) PCT).

PATENT COOPERATION TREATY

WO 01/24791
PCT/EP00/10084

PCT

From the INTERNATIONAL BUREAU

To:
DUFRESNE, Guillaume
Warner-Lambert Company
Pfizer Global Research & Development
Fresnes Laboratories
3-9, rue de la Loge, Boîte Postale 100
F-94265 Fresnes Cedex
FRANCE

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

Date of mailing (day/month/year) 12 April 2001 (12.04.01)	
Applicant's or agent's file reference A000005-PCT2	**IMPORTANT NOTICE**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/EP00/10084	09 October 2000 (09.10.00)	07 October 1999 (07.10.99)

Applicant
WARNER-LAMBERT COMPANY et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,KP,KR,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AE,AG,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,BZ,CA,CH,CN,CR,CU,CZ,DE,DK,DM,DZ,EA,EE,EP,ES,FI,GB,GD,GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,MZ,NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,
   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   12 April 2001 (12.04.01) under No. WO 01/24791

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Gen va 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer
J. Zahra

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

DUFRESNE, Guillaume
Warner-Lambert Company
Pfizer Global Research & Development
Fresnes Laboratories
3-9, rue de la Loge, Boite Postal 100
F-94265 Fresnes Cedex
FRANCE

Date of mailing (day/month/year) 09 January 2001 (09.01.01)	
Applicant's or agent's file reference A000005-PCT2	**IMPORTANT NOTIFICATION**
International application No. PCT/EP00/10084	International filing date (day/month/year) 09 October 2000 (09.10.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 07 October 1999 (07.10.99)
Applicant WARNER-LAMBERT COMPANY et al	

EXPRESS MAIL NO. EF220793517US
A0000005/2-01-MG

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
07 Octo 1999 (07.10.99)	60/158,271	US	21 Dece 2000 (21.12.00)

Th International Bureau of WIPO
34, ch min des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Elisabeth KÖNIG

Telephone No. (41-22) 338.83.38

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

DUFRESNE, Guillaume
WARNER-LAMBERT COMPANY
Pfizer Global Research &
Fresnes Laboratories
3-9, rue de la Loge, B.P. 100
F-94265 Fresnes Cedex
FRANCE

PCT

WRITTEN OPINION

(PCT Rule 66)

délai 06.12.2001.

Date of mailing *(day/month/year)*	06.09.2001
Applicant's or agent's file reference: A000005-PCT2 J7885 - BD -	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/10084	09/10/2000	07/10/1999

International Patent Classification (IPC) or both national classification and IPC

A61K31/195

Applicant

WARNER-LAMBERT COMPANY et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 07/02/2002.

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner

Pilling, S

Formalities officer (incl. extension of time limits)

Hundt, D
Telephone No. +49 89 2399 8042

EXPRESS MAIL NO. EF220793517US
A0000005/2-01-MG

I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-12 as originally filed

Claims, No.:

1-11 as originally filed

Drawings, sheets:

1/1 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-9,

because:

☒ the said international application, or the said claims Nos. 1-9 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims
Inventive step (IS)	Claims 1-11

Industrial applicability (IA) Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1 to 9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2. The present application relates to the treatment of psychiatric disorders using a synergistic combination of an NK_1 receptor antagonist and a GABA analogue.

3. Claims 1 to 9 relate to methods of treatment of the human or animal body by therapy. In this regard, for the assessment of these claims with respect to industrial applicability, no unified criteria exist in the PCT. Furthermore, patentability can be dependent on the formulation of the claims. The EPO, for example does not recognize as industrially applicable, the subject matter of claims directed to a method of treatment of the human or animal body or to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D5 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

5. None of the documents cited in the ISR discloses treatment of psychiatric disorders using a combination of an NK_1 receptor antagonist and a GABA analogue. Thus, the subject matter of the present claims is new (Article 33(2) PCT).

6. The closest prior art in respect of the present claims appears to be any of documents D1 to D5. These documents show that the separate use of either (i) NK_1 receptor analogues (see documents D1 to D2) or (ii) GABA analogues such as gabapentin or pregabalin (see documents D3 to D5) for the treatment of psychiatric disorders such as anxiety, depression and panic is known. Despite numerous references in the present description to a synergistic effect associated with the combined use of these active agents in treating psychiatric disorders, there seems to be no clear evidence therein to support the existence of any such synergistic effect. In particular, the method of present Example 1 only appears to have been carried out using the Applicant's preferred NK_1 receptor antagonist, *i.e.* CI-1021. There seem to be no experimental results relating to the combined use of the latter compound with GABA analogues. Hence, it is considered that the alleged synergistic effect has not yet been made credible and cannot presently be used to support inventive step of the present claims.

7. Hence, the objective technical problem to be solved by the subject matter of the present application appears to be "*how to provide alternative compositions for the treatment of psychiatric disorders*". The Applicant is advised that in general it is not considered inventive to combine active agents for the treatment of a particular disease wherein (i) said active agents were individually known for the treatment of said disease and (ii) wherein the combination thereof has no surprising technical effects, *e.g.* synergistic effect(s). In this regard, it is common general knowledge in the medical art that treatments may be combined and it would be expected that (at least additive) therapeutic benefits would be associated with the use of such combined treatment. Hence, in the absence of any proven surprising technical effect(s) associated with the use of the NK_1 receptor antagonists in combination with the GABA analogues to treat psychiatric disorders, it is considered that the present claims merely define obvious combined treatments. Thus, the subject matter of Claims 1 to 11 is not inventive (Article 33(3) PCT).

Re Item VII

Certain defects in the international application

8. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in documents D1 to D5 is not mentioned in the description, nor are

these documents identified therein.

Re Item VIII
Certain observations on the international application

9. The statement that "*In a further aspect of the present invention, there is provided a pharmaceutical composition for the treatment..Etc*" (see page 6 lines 9 to 11) is inconsistent with the invention as claimed that relates only to methods and uses. Hence this statement casts doubt on the scope of the claims leading to lack of clarity thereof (Article 6 PCT). Similar considerations apply in respect of the statement on page 9 (see lines 1 to 2).

these documents identified therein.

Re Item VIII
Certain observations on the international application

9. The statement that "*In a further aspect of the present invention, there is provided a pharmaceutical composition for the treatment..Etc*" (see page 6 lines 9 to 11) is inconsistent with the invention as claimed that relates only to methods and uses. Hence this statement casts doubt on the scope of the claims leading to lack of clarity thereof (Article 6 PCT). Similar considerations apply in respect of the statement on page 9 (see lines 1 to 2).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
A000005-PCT2		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 00/ 10084	09/10/2000	07/10/1999
Applicant		
WARNER-LAMBERT COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figur .

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

Form PCT/ISA/210 (first sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

Internatic Application No
PCT/EP 00/10084

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/195 A61K31/404 A61K31/40 A61P25/18 A61P25/24
A61K45/06 //(A61K31/40,31:195)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal, MEDLINE, EMBASE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 24439 A (ELLIOTT JASON MATTHEW ;HOLLINGWORTH GREGORY JOHN (GB); KULAGOWSKI) 11 June 1998 (1998-06-11) page 3, line 20 - line 27 page 6, line 21 -page 7, line 31 Assay 4 ---	1-11
Y	WO 98 15277 A (CARLSON EMMA JOANNE ;MERCK SHARP & DOHME (GB); RUPNIAK NADIA MELAN) 16 April 1998 (1998-04-16) page 3, line 27 -page 4, line 6 page 5, line 30 -page 6, line 10 Assay 2 ---	1-11
Y	US 5 510 381 A (PANDE ATUL C) 23 April 1996 (1996-04-23) column 1, line 46 -column 2, line 54 --- -/--	1-11

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 January 2001	07/02/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Pilling, S

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	US 5 792 796 A (BROWN JASON PETER ET AL) 11 August 1998 (1998-08-11) column 2, line 33 - line 37	1-11

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